July 16, 1943

Dr. S. E. Luria
Department of Biology
Princeton University
Princeton, New Jersey

Dear Luria:

It is a little difficult for me to answer your letter without having your paper before me. Particularly, I cannot recall how you showed that all offspring of a bacterium resistant to virus are also resistant; and I'd like to know whether your proof shows this is independent of contact with virus, i.e., whether some clones are genetically resistant before this contact.

You will see my objections better if I tell you briefly our findings with Paramecium. We injected a race into a rabbit and obtained an antiserum specific for this race. When many clones of this race were subjected to antiserum, some were 100% sensitive and never showed any resistant individuals; other clones had small proportions of resistant cells, the proportions differing in different clones. In the 100% sensitive clones, we were never able to obtain resistant cells by subjecting them to antiserum or otherwise. In the clones containing resistant individuals we showed that this resistance (prior to subjection to the antiserum) was non-hereditary in essentially the following way: many individuals were isolated; after each cell divided once, one daughter cell was tested, the other one was not; of the tested cells, some were resistant, others were not; the untested sister cell was allowed to divide again and again one product of division was tested and the other was not; this time all the tests were negative, showing that the sister cell of a resistant cell is not resistant. However, the cells which are resistant, though not hereditarily so, can be made hereditarily resistant by subjecting them to the antiserum. This acquired resistance was followed in many lines of descent. In some it disappeared after a small number of fissions, in others it persisted longer and in some it was persistant as long as we followed the cultures, - for over 300 successive fissions in daily isolation pedigreed cultures. We showed that the "inherited" "acquired" character was <u>not</u> an ordinary mutation by making a number of kinds of crosses: resistant x sensitive, resistant by resistant, etc. In <u>every</u> kind of cross, and also from autogamy alone, the resistance was invariably lost in less than 8 fissions after fertilization. It was thus <u>not</u> inherited at all in sexual reproduction of any kind, but appeared to be capable of very long inheritance in asexual reproduction. We also made many other kinds of experiments on the acquirement, persistence and loss of the resistance, but the essential facts from your point of view are those I have just stated.

You see the alternative you designated as " a little unpleasant" is the very one we found. I may say that I was not looking for such a result, have always been to say the least suspicious of this kind of thing, and because of my prejudices was prevented from discovering what was taking place for a considerable time.

I hope you are getting better adjusted to the heat and can do your work in spite of it. It is terrible here, but we manage to survive and keep too busy.

Best wishes,

Yours,

T. M. Sonneborn

TMS:lm